

Application No.: 10/652,334  
Amendment and Response dated March 30, 2005  
Reply to Office Action of February 7, 2005  
Docket No.: 1368-12 CON  
Page 2

**Amendments to the Specification**

Please replace the abstract with the following abstract:

--An isolated multiprotein complex of *S. cerevisiae* components is provided that is effective to modulate peptidyl transferase activity during translation. This complex includes a Modulator of Translation Termination protein (Mtt1p, also referred to as helicase B), a Upf1 protein, a peptidyl eukaryotic release factor 1 (eRF1) and a peptidyl eukaryotic release factor 3 (eRF3). --

Please replace the paragraph beginning at page 7, line 1, with the following rewritten paragraph:

-- This invention provides a method of identifying genes which are involved in modulation of the fidelity of translation termination, which comprises: a) isolating a gene of interest; and b) determining whether the gene of interest comprises motifs I-IX, wherein if the gene comprises any one of the nine motifs the gene modulates translation termination. In one embodiment motif I comprises the sequence: GppGKTxT-X(n) (SEQ ID NO:1). In another embodiment motif II comprises the sequence riLxcaSNxAvDxl-X(n) (SEQ ID NO:2). In another embodiment motif III comprises the sequence vviDExxQaxxxxxiPi-X(n) (SEQ ID NO:3). In another embodiment motif IV comprises the sequence xxil aGDxxQLp-X(n) (SEQ ID NO:4). In another embodiment motif V comprises the sequence lxx SLF erv-X(n) (SEQ ID NO:5). In another embodiment motif VI comprises the sequence LxxQYRMhpxisefpxYxgxL-X(n) (SEQ ID NO:6). In another embodiment motif VII comprises the sequence IgvitPYxxQvxxl-X(n) (SEQ ID NO:7). In another embodiment motif VIII comprises the sequence vevxtVDxFQGreKdxlilSc VR-X(n) (SEQ ID NO:8). In another embodiment motif IX comprises the sequence iGFLwdxRRINValTRak (SEQ ID NO:9). --

Please replace the paragraph beginning at page 38, line 9, with the following rewritten paragraph:

-- This invention provides a method of identifying genes which are involved in modulation of translation termination, which comprises: a) isolating a gene of interest; and b) determining

Application No.: 10/652,334

Amendment and Response dated March 30, 2005

Reply to Office Action of February 7, 2005

Docket No.: 1368-12 CON

Page 3

whether the gene of interest comprises motifs I-IX, wherein if the gene comprises any one of the nine motifs the gene modulates translation termination. In one embodiment motif I comprises the sequence: GppGTKTxT-X(n) (SEQ ID NO:1). In another embodiment motif II comprises the sequence riLxcaSNxAvDxl-X(n) (SEQ ID NO:2). In another embodiment motif III comprises the sequence vviDExxQaxxxxxiPi-X(n) (SEQ ID NO:3). In another embodiment motif IV comprises the sequence xxi1 aGDxxQLp-X(n) (SEQ ID NO:4). In another embodiment motif V comprises the sequence lxx SLF erv-X(n) (SEQ ID NO:5). In another embodiment motif VI comprises the sequence LxxQYRMhpxisefpxYxgxL-X(n) (SEQ ID NO:6). In another embodiment motif VII comprises the sequence IgvitPYxxQvxxl-X(n) (SEQ ID NO:7). In another embodiment motif VIII comprises the sequence vevxtVDxFQGreKdxlilSc VR-X(n) (SEQ ID NO:8). In another embodiment motif IX comprises the sequence iGFLxdxRRINVaTRak(SEQ ID NO:9). Capitol letters represent a position in the primary sequence whose specific amino acid residue is very highly conserved among member of this group. Lowercase letters represent a position in the primary sequence whose chemical properties are conserved but not necessarily the exact identity. - -

Please replace the paragraph beginning at page 57, line 17, with the following rewritten paragraph:

- - Eight conserved motifs are associated with all superfamily group I helicases (Gorbalenya, 1988, Koonin, 1992). Within these eight motifs, a limited number of residues is conserved among all superfamily group I helicases. Although these 8 motifs are spaced variably from protein to protein, according to the crystal structure of 2 different superfamily group I helicases, these conserved residues are all in close proximity in 3 dimensions (2 crystal structure papers). A more careful analysis of the genes with similarity to UPF1 identifies this group as a subclass of superfamily group I which, the UPF1-like subclass. The distinguishing feature of this subclass is a more extensive homology surrounding the conserved residues in motifs II, IV, V and VI (FIG. 2) which has been noted previously (Perlick et al. 1996). Furthermore two additional motifs within this domain are conserved among these five genes. The first is located between motifs III and IV (consensus lexSLFervl (SEQ ID NO:10), FIG. 2) and the second is located between

Application No.: 10/652,334

Amendment and Response dated March 30, 2005

Reply to Office Action of February 7, 2005

Docket No.: 1368-12 CON

Page 4

motifs IV and V (consensus IgvitpYxaQ (SEQ ID NO:11); FIG. 2), referred as motif IIIa and IVa, respectively. These additional motifs are present in the human homolog of the Upf1 gene as well. Of these five yeast genes, Dna2p is the poorest fit to the consensus, and omission of this sequence yields a tighter consensus. Two other superfamily group I helicases from yeast, Pif1 and RadH, and two well characterized group I helicases from E. coli, Rep and uvrD, could not be aligned to these five sequences under these parameters, indicating that the homology is not general to all superfamily group I helicases, thus evidence for a distinct subclass. - -